

Analysis of the correlation between COVID-19 infection frequency and disease severity and mortality in relation to ABO and RH blood groups

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ABSTRACT

Aims: The etiology of the COVID-19 pandemic and the factors that predispose individuals to the disease remain little comprehended. Research indicates significant variability in outcomes related to blood types and COVID-19. These researches have examined ABO and Rhesus (Rh) blood types as different datasets. Our research is an unprecedented study that investigates the correlation between developing COVID-19 and/or disease severity/death by analyzing ABO and Rh blood groups concurrently.

Methods: This study retrospectively included 461 RT-PCR-diagnosed COVID-19 patients and 46 healthy volunteers aged 18 or older with known blood types from April 2020 to December 2020. All demographic and medical data came from electronic medical records (EMR). Rh and ABO blood types were established via card tests with microplates (forward and reverse grouping). Patients were grouped by clinical outcome and COVID-19 positivity. In SPSS 26, descriptive statistics, one-way ANOVA, Kruskal-Wallis, student's T test, Mann-Whitney U test, and Chi-square test assessed regularly distributed and non-normally distributed characteristics.

Results: The age distribution of the patients (62 ± 13) was comparable to that of the control group (64 ± 14) ($p=0.295$). No significant differences were seen between the groups regarding sex and blood group distribution ($p=0.204$ and $p=0.087$, respectively). Analysis of individuals by blood types revealed no significant differences in the incidence of COVID-19, age, sex, and clinical course ($p=0.603$, $p=0.244$, $p=0.272$, and $p=0.810$, respectively).

Conclusion: Our investigation demonstrated that, contrary to the current literature, there is no correlation between developing COVID-19 and/or the severity of the disease or mortality across the eight blood groups classified by ABO and Rh combinations. This may signify a realistic consequence or could be linked to genetic profiles. We contend that, contrary to assertions in the literature, there is no link between ABO and Rh blood types and the incidence, severity, or mortality of COVID-19.

Keywords: COVID-19, blood group antigens, SARS-CoV-2, Rh-Hr blood-group system, ABO blood-group system

INTRODUCTION

Following the initial identification of COVID-19 in Wuhan, China, the advent of the novel SARS-CoV-2 coronavirus precipitated a global public health catastrophe characterized by significant morbidity and mortality that swiftly overwhelmed healthcare systems worldwide. Nonetheless, the disease's impact exhibits significant diversity across countries and geographic regions for reasons that remain inadequately comprehended. In addition to variations in economic, sociological, behavioral, and political responses to the pandemic, genetic variables may potentially independently influence outcomes. Consequently, shortly after the onset of the pandemic, a publication from Wuhan, China, indicated an elevated risk of infection for those with blood group A, whereas conversely, individuals with blood group O exhibited a reduced risk.¹ Subsequently, connections with ABO and Rhesus (Rh) blood groups have been documented in numerous

papers globally.²⁻⁷ The influence of ABO and Rh blood types on SARS-CoV-2 infection and COVID-19 outcomes, as well as its implications for the pandemic's progression in various global locations and its potential significance for patient care, require more evaluation.

The findings concerning the relationship between ABO and Rh blood groups are inconsistent. Several studies have not established a definitive correlation between blood type and susceptibility to COVID-19, or have reported varying results. This study will examine the relationship between blood groups and COVID-19, drawing on existing literature to elucidate the potential effects of various blood groups on susceptibility to the virus and the progression of the disease. Also, the literature has analyzed COVID-19 in relation to ABO and Rh groups independently. Conversely, our study was conducted

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utilizing both ABO and Rh systems, encompassing 8 blood types. We assert that we will enhance the literature in this context.

METHODS

Study Population

This study retrospectively included 461 COVID-19 patients diagnosed with RT-PCR and 46 healthy participants between April 2020 and December 2020, all of whom were over 18 years old and had known blood types. Healthy people were chosen to match the patients in terms of sex and age distribution. Individuals lacking a documented blood type in their medical records were excluded from the study. There was no individual with COVID-19 vaccine history. The patients were further categorized into subgroups: outpatients, hospitalized individuals, and died patients. All clinical information were obtained from medical records. After obtaining a COVID-19 work permit and IRB confirmation from the Ministry of Health of Türkiye, the study was initiated after receiving approval from the Amasya University Non-interventional Clinical Researches Ethics Committee (Date: 11.06.2020, Decision No: 7/55). The Helsinki Declaration of Human Rights was followed.

Study Design

All demographic and medical data was extracted from electronic medical records (EMR). The Rh and ABO blood types were determined using card tests with microplate method (forward and reverse grouping techniques). Patients were categorized based on their clinical course and COVID-19 positivity. First, individuals were divided as COVID-19 PCR positives and negatives. Then, outpatients, inpatients, and deceased individuals were classified into primary categories. Comparisons were conducted between the control group and the patient groups based on all blood types. The relationship between blood groups and the frequency of disease occurrence and clinical progression was investigated.

Statistics Analysis

The study used SPSS version 26.0 for analyses, assessing parameters with normal distribution using Shapiro-Wilk's test. Descriptive statistics, one-way ANOVA, Kruskal-Wallis, student's T test, Mann-Whitney U test, and Chi-square test were used to compare normally distributed and non-normally distributed parameters. A p-value below 0.05 was considered significant.

RESULTS

The age distribution of the patients (62 ± 13) did not differ from the control group (64 ± 14) ($p=0.295$). Additionally, no differences were found between the groups in terms of sex and blood group distribution ($p=0.204$, and $p=0.087$, respectively). Upon analyzing individuals by blood types, we observed no significant differences in the incidence of COVID-19, age, sex, and clinical course ($p=0.603$, $p=0.244$, $p=0.272$, and $p=0.810$, respectively). Among all categories, the A Rh positive blood group was the most prevalent, whereas the A Rh negative was the least prevalent. The second most prevalent blood type is O Rh positive (Table). No correlation was identified between blood types and the severity or incidence of disease.

DISCUSSION

Blood groups and COVID-19 positivity

Researchers indicated that blood type A is correlated with the greatest likelihood of SARS-CoV-2 infection.⁸⁻¹⁰ A preliminary study conducted in Wuhan, China, indicated a correlation between blood type A and COVID-19, highlighting that females with blood type A exhibited increased susceptibility to infection.⁸ Subsequent research indicated that people with blood type A exhibited markedly increased odds of contracting SARS-CoV-2 infection in comparison to individuals with non-A blood types.^{1,8,9} Numerous studies indicate that individuals with blood type O exhibit markedly reduced probabilities of infection, implying that blood type O may serve as a preventive factor against infections.^{11,12} One multivariate analysis of 14,112 COVID-19-positive individuals found that blood types A, AB, and B were more common than O after correcting for race and ethnicity.¹³ A study in China found that blood type increases COVID-19 risk in retrospective research. Infection risk was lower for blood type O patients than non-O patients and greater for blood type A patients than all other groups.⁶ Although most studies have found that having blood type O protects against COVID-19,¹¹ researchers still can't agree on which blood types are more vulnerable. Furthermore, several studies have suggested that blood types B and AB are at a high risk, in contrast to those that identify blood type A as the most at-risk group.¹² A study indicated that blood types B and AB were correlated with increased odds of testing positive for SARS-CoV-2 infection, while blood type O was linked to decreased odds of testing positive. Nevertheless, the authors identified no association between blood type A and positive testing rates.¹⁴ According to the findings of our research, we did not discover a correlation between blood types and the probability of getting COVID-19. This is with all due respect to the research that was already conducted. Several distinct conclusions were already being indicated by the literature data in an inconsistent manner. After taking into consideration all of this evidence, we have arrived at the conclusion that there is no correlation between blood types and COVID-19 infections.

Blood Groups and Clinical Outcome

A study indicated that patients with blood type A exhibited a reduced risk of intubation and mortality compared to those with blood type O, while those with blood type AB demonstrated an increased risk of intubation and death. Furthermore, those with blood type B had elevated intubation rates, although experienced reduced mortality in comparison to those with blood type O.¹³ In contrast, population-based cohort research indicated that individuals with blood type O have a reduced chance of acquiring severe illnesses or mortality compared to all other blood types.¹² In a study employing Spearman's rank coefficient analysis on COVID-19 patients, researchers discovered that blood type O conferred protection against COVID-19 mortality, while blood type B exhibited a stronger correlation with infection and mortality rates.¹⁴ A multicenter retrospective analysis indicated that individuals with blood type A or AB faced an increased risk of needing mechanical ventilation compared to those with blood type O or B, even after controlling for sex, age, and other variables. Following the adjustments, there were no observed differences in the median duration of ICU stay or the likelihood of ICU discharge or extubation. No correlation was found between

Table. The prevalence and intensity of diseases among persons categorized by blood groups, including numerical and percentage ranges

					Count n	Group n%	Total n%
RT-PCR	Non-COVID-19	Post-treatment course	Death	Blood group	0 Rh (-)	0	0.0%
					0 Rh (+)	1	0.2%
					A Rh (-)	0	0.0%
					A Rh (+)	3	0.6%
					B Rh (-)	1	0.2%
					B Rh (+)	2	0.4%
					AB Rh (-)	0	0.0%
					AB Rh (+)	1	0.2%
			Discharged	Blood group	0 Rh (-)	0	0.0%
					0 Rh (+)	3	0.6%
					A Rh (-)	1	0.2%
					A Rh (+)	12	2.5%
					B Rh (-)	0	0.0%
					B Rh (+)	3	0.6%
					AB Rh (-)	0	0.0%
					AB Rh (+)	3	0.6%
			No hospitalization	Blood group	0 Rh (-)	0	0.0%
					0 Rh (+)	2	0.4%
					A Rh (-)	0	0.0%
					A Rh (+)	10	2.1%
					B Rh (-)	0	0.0%
					B Rh (+)	1	0.2%
					AB Rh (-)	0	0.0%
	COVID-19	Post-treatment course	Death	Blood group	AB Rh (+)	0	0.0%
					0 Rh (-)	3	0.6%
					0 Rh (+)	27	5.7%
					A Rh (-)	8	1.7%
					A Rh (+)	77	16.2%
					B Rh (-)	3	0.6%
					B Rh (+)	9	1.9%
			Discharged	Blood group	AB Rh (-)	1	0.2%
					AB Rh (+)	9	1.9%
					0 Rh (-)	4	0.8%
					0 Rh (+)	61	12.8%
					A Rh (-)	17	3.6%
					A Rh (+)	128	26.9%
					B Rh (-)	4	0.8%
					B Rh (+)	37	7.8%
			No hospitalization	Blood group	AB Rh (-)	4	0.8%
					AB Rh (+)	20	4.2%
					0 Rh (-)	0	0.0%
					0 Rh (+)	7	1.5%
					A Rh (-)	2	0.4%
					A Rh (+)	7	1.5%
					B Rh (-)	1	0.2%
					B Rh (+)	1	0.2%
					AB Rh (-)	0	0.0%
					AB Rh (+)	2	0.4%

RT-PCR: Reverse-transcriptase polymerase chain reaction, Rh: Rhesus

blood type and mortality.¹⁵ Our findings indicate that there is no correlation between outpatient treatment of patients, the clinical conditions necessitating hospitalization, the requirement for intensive care, or mortality rates and blood groups. While there are considerable investigations in the literature regarding various blood groups and their associated clinical outcomes, these studies seem to lack consistency in

both hypothesis formulation and scientific reasoning. Our findings indicate that there is no correlation between blood groups and the clinical outcomes of COVID-19.

Rh Factor and COVID-19

Given that blood types are categorized as positive or negative based on the presence of the Rh factor protein, it is important to

explore the relationship between Rh and COVID-19 infection. A study indicated that Rh (+) correlated with increased odds of testing positive, as well as elevated risks of intubation and mortality.¹² A separate investigation by revealed that Rh (–) patients exhibited a 2.7% reduced risk of initial infection, intubation, and mortality after controlling for sex, age, and other demographic factors.¹³ A research study conducted by Ray et al.¹⁶ also suggested that those with Rh (–) blood type exhibited reduced susceptibility to SARS-CoV-2 infection, particularly among individuals with O-negative blood type. Nonetheless, a separate hematological investigation carried out in Sudan suggested that individuals with the O-positive blood group exhibit the least likelihood of experiencing severe symptoms, whereas the authors concurred that those with A-positive blood type are the most susceptible upon exposure to the virus.¹⁷ Our data analysis revealed, in contrast to existing literature, that there is no correlation between Rh status and the incidence and/or severity of clinical outcomes related to COVID-19. The absence of statistical significance in our study data could be associated with the characteristics of our patient population, or it is possible that the disease does not genuinely correlate with the Rh factor.

Limitations

The main drawback of our study was that it was conducted as a single-centered investigation within a single region. It is our conviction that studies carried out across multiple centers, encompassing various ethnic regions and diverse patient populations, will yield greater benefits.

CONCLUSION

Our study revealed that, contrary to existing literature, there is no association between contracting COVID-19 and/or the severity of the disease or death across the 8 blood groups defined by the ABO and Rh combinations. This may represent a plausible outcome or could potentially be associated with genetic profiles. We assert that, contrary to claims in the literature, there is no correlation between ABO and Rh blood classes and the incidence, severity, or mortality of COVID-19.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Amasya University Non-interventional Clinical Researches Ethics Committee (Date: 11.06.2020, Decision No: 7/55).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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